Unusual severe hypercholesterolaemia and xanthomas in a patient with hepatolithiasis

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CASE REPORT

A 47-year-old woman had undergone cholecystectomy for gallstones in December 1994 at a local hospital. In December 1995 she presented at the surgical outpatient department with intermittent right upper quadrant pain. Laboratory studies revealed serum albumin 4.3 g/dl (normal 3.5–5.3 g/dl), total cholesterol 307 mg/dl (normal <200 mg/dl), total bilirubin 1.8 mg/dl (normal 0.0–1.3 mg/dl), alkaline phosphatase 602 U/litre (normal 28–94 U/litre), aspartate aminotransferase (AST) 129 U/litre (normal 0–34 U/litre), and alanine aminotransferase (ALT) 196 U/litre (normal 0–36 U/litre). Liver sonography revealed multiple stones in dilated intrahepatic and common hepatic ducts. However, the patient did not receive further studies of her hepatolithiasis at that time. The patient underwent percutaneous transhepatic cholangiostomy drainage for intrahepatic stones and jaundice in a medical centre in January 1998. In February 1998 she was transferred to the surgical department because of persistent jaundice. Physical examination revealed that the woman was markedly icteric, with an old scar on the right upper abdominal wall, and no xanthoma was found on the body. Laboratory results included that serum albumin was 4.1 g/dl, total cholesterol was 256 mg/dl, total bilirubin was 12 mg/dl, alkaline phosphatase was 512 U/litre, AST was 101 U/litre and ALT was 100 U/litre. Cholangiogram showed a dilated biliary tree with multiple stones in intrahepatic ducts, common hepatic ducts and the common bile duct.

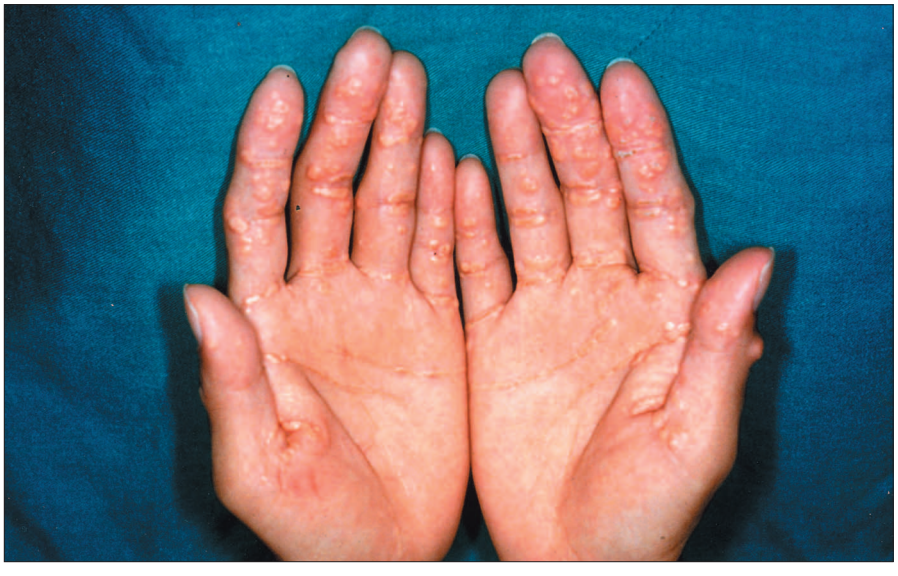
The patient underwent choledocholithotomy with choledochojejunostomy, Roux-en-Y jejunojejunostomy, and a T-tube drainage in the common bile duct in February 1998. The liver biopsy displayed cholestasis and no cirrhotic change. Following surgery the woman was regularly followed up in the outpatient department and intrahepatic stones were removed intermittently via a T-tube. Cholangitis was noted during follow-up, and the patient received five 7-day courses of amoxicillin 1000 mg/day in divided doses from September 1998 to February 1999. The jaundice was persistent during follow up, and painful xanthomas developed on both hands and elbows in February 1999, particularly on the palmar side (*Figure 1*). Laboratory tests revealed significantly raised serum total cholesterol, total bilirubin, and alkaline phosphatase levels (*Figure 2*). Lipoprotein electrophoresis displayed that total cholesterol was 1046 mg/dl, β-lipoprotein (low-density lipoprotein) was 72.6% (normal 36–61%), pre-β-lipoprotein (very low-density lipoprotein) was 15.7% (normal 2–30%), and α-lipoprotein (high-density lipoprotein) was 11.7% (normal 22–48%). Subsequently, the patient received no more amoxicillin, and the xanthomas gradually regressed. Total regression of hypercholesterolaemia and xanthomas was achieved in November 2000, at which point total serum cholesterol was 200 mg/dl, total bilirubin was 12 mg/dl, and alkaline phosphatase was 676 U/litre.

INTRODUCTION

The association between high plasma cholesterol levels and obstructive jaundice is well recognized. Switzer (1967) found abnormal lipoprotein levels among patients with primary biliary cirrhosis (PBC) by removing the normal low-density lipoprotein (LDL) from the low-density fraction with antibodies to normal LDL. Seidel et al (1970) named the abnormal lipoprotein 'lipoprotein-X' (LP-X).

Amoxicillin-clavulanic acid-associated cholestasis has been reported (Dowsett et al, 1989), but amoxicillin alone is a rare cause of liver dysfunction. This study describes a patient with secondary cholestasis and jaundice caused by hepatolithiasis, who developed unusual severe hypercholesterolaemia and painful xanthomas involving the hands and elbows during amoxicillin treatment post-surgery.

Figure 1. Well-demarcated, hard, pebble-like xanthomas on the palms of the hands.



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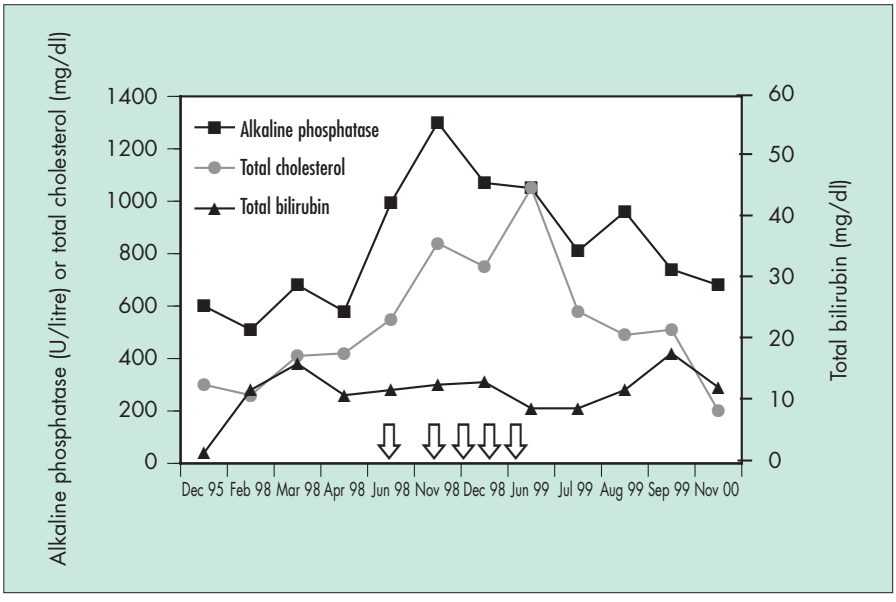

Figure 2. Time-sequence changes in plasma total cholesterol, total bilirubin and alkaline phosphatase levels, and time of amoxicillin-treatment (⇩).

DISCUSSION

The clinical presentation of this cholestatic patient with hypercholesterolaemia was unusual. Her cholesterol level rose from 256 mg/dl to 1046 mg/dl during amoxicillin treatment post-surgery, and xanthomas developed rapidly. The xanthomas in this patient were painful, well-demarcated, hard, pebble-like, and extended beyond the palmar creases. The xanthomas thus resembled those present in PBC, and were different from those associated with familial hypercholesterolaemia. In this study, agarose gel lipoprotein electrophoresis displayed the presence of an abnormal broad band in the β-position, suggesting the presence of LP-X.

The development of hypercholesterolaemia in patients with PBC has been extensively studied, but few investigators have reported patients with secondary cholestatic liver disease having xanthomas. A literature review revealed only one patient with chronic cholestasis of pancreatic origin, who had tuberous xanthoma, xanthoma striatum palmare and hypercholesterolaemia (Vaillant et al, 1989).

Previous studies have reported amoxicillin-clavulanic acid-induced intrahepatic cholestasis. The mechanism of hepatic dysfunction caused by amoxicillin-clavulanic acid is unclear but is probably immunological (Dowsett et al, 1989). Davies et al (1994) described a female with normal liver function who received amoxicillin for upper respiratory tract infection, and rapidly progressing acute cholestasis developed within a week of drug exposure. In this study, inadvertent treatment with amoxicillin in the secondary cholestatic patient aggravated the cholestasis and caused severe hypercholesterolaemia and xanthomas. Hepatolithiasis is common in South-east Asia (Nakayama et al, 1986), so amoxicillin should not be used to treat infections in these patients. HM

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